

REMARKS

In view of the above amendment and following remarks, the Examiner is requested to allow claims 1-23, the only claims pending and under examination in this application.

Formal Matters

The Applicants acknowledge and thank the Examiner for the withdrawal of the rejections under 35 U.S.C. §112, first paragraph for lack of enablement and the rejection under 35 U.S.C. §103.

In light of the following discussion, it is submitted that the instant claims are in proper form for allowance, which action is respectfully requested.

Claim Rejections – 35 U.S.C. § 112

Claims 1-23 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. It is asserted that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Specifically, the Examiner states that it is unclear as to whether the Applicants had possession of the invention with regard to complex mixtures of any kind of protein, encompassing any glycopeptide of any molecular mass and composition; including any kind of saccharide attached by multiple possible bonds to the peptide; including isolation from mixtures with low concentrations of glycopeptide; encompassing peptides and glycopeptides with any type of functional groups therein, and proteins with multiple glycosylation sites.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19

USPQ2d at 1116. The Applicants submit that the instant specification more than adequately demonstrates that the inventor of the present invention had possession of the claimed invention.

In evaluating whether adequate written description exists, guidelines have been implemented by the Office. The Written Description Guidelines state:

- (1) There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed;
- (2) The Examiner has the initial burden of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims;
- (3) Consequently, rejection of an original claim for lack of written description should be rare;
- (4) An Examiner should review the entire application to understand how Applicant provides support for the claimed invention; and
- (5) Such a review is conducted *from a standpoint of one of skill in the art at the time the application was filed and should include a determination of the field of the invention and the level of skill and knowledge in the art* (emphasis added).¹

As will be demonstrated below, applying the guidelines to the facts of the present application results in a conclusion that the inventor had possession of the claimed invention.

With regard to the level of skill in the art, the ordinary artisan performing the instant method is likely to be a trained chemist or biochemist with an advanced degree in the relevant discipline, or an artisan well-trained in the techniques and troubleshooting of protein purification. As such, the ordinary artisan can be relied upon, where necessary, to be able to practice the routine experimentation described in the instant specification.

¹ Written Description Guidelines, MPEP §2163(II)(A)(1) and (2).

The Examiner states that the claimed method is broadly applicable, and the Applicants concur. As established in the previous Reply, the technique is applicable to the separation of any sample containing a mixture of glycosylated and deglycosylated proteins, including O-glycosylated proteins, N-glycosylated proteins, C-mannosylated, phosphoglycosylated, etc. The β -elimination reactions are known to those of skill in the art and reaction conditions that can provide for β -elimination at different glycosylation sites can readily be determined by those of skill in the art without undue experimentation.

The Examiner states that a single example is provided by the Applicants describing the separation of a single unspecified protein sample, and that it is unclear whether the Applicants had possession of the invention with regard to a variety of parameters of the biological sample containing target glycosylated protein or proteins.

The Written Description Guidelines state that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species; and that a "representative number of species" means that the species which are adequately described are representative of the entire genus. The Written Description Guidelines state that there may be situations in which one species adequately supports a genus; and that what constitutes a "representative number" is an inverse function of the skill and knowledge in the art.² The Applicants respectfully submit that the claimed method is capable of isolating any glycosylated protein that may be present in a biological sample, and, as such, the specific identity of the exemplified target protein is unnecessary in order for the example to be informative to one of ordinary skill in the relevant art.

The Applicants firstly note that the specification indicates that targets will be found "in a biological sample" (specification, page 18, first paragraph). As such, the target proteins do not include an infinite number of glycopeptides of any mass or composition, nor an infinite number of saccharides with any possible functional group

² MPEP §2163 (II)(A)(3)(a)(ii).

attached by an endless variety of chemical bonds, such as might be found in a synthetic library.

Rather, as established in the previous Reply, the variety of types of glycosylation linkages found in biological samples has been well characterized and experimentation required to separate the various types is within realm of routine experimentation.

With regard to complex mixtures of proteins found in biological samples, and cases in which the target may be rare, the instant specification describes optionally subjecting the biological sample to one or more separation processes, such as digesting with one or more proteases before contacting the mixture with the resin. In this embodiment, glycosylated or unglycosylated proteins in the mixture have a molecular weight of about 5000 daltons or less after digestion. In typical embodiments, prior to contacting the mixture with the resin, the mixture may be treated to dephosphorylate the proteins in the mixture, e.g. by treating the mixture with a phosphatase to remove phosphate moieties from the proteins. Conditions and protocols for performing the dephosphorylation are known in the art.

The specification further describes, after releasing the deglycosylated protein from the solid support, subjecting it to further purification and/or analysis, where such further purification and/or analysis may include mass spectrometry, HPLC, fluorimetric analysis, gel electrophoresis, or any other purification and/or analysis known to the art (page 20, lines 13-16). As such, methods for coping with complex mixtures and rare targets are more than adequately provided to the ordinarily skilled artisan.

With regard to variation in mass of potential target proteins, the specification throughout describes the result of the β -elimination reaction as a target protein covalently bonded to the solid support. As is well known in the art, the covalent bond is the strongest known organic chemical bond and, as such, provides for a very wide toleration of mass in the target protein. As such, the methods described by the

instant specification are sufficient for the isolation of glycosylated proteins in biological samples.

With regard to identities of the saccharide group, the specification indicates that the saccharide monomer subunits typically are selected from N-acetyl glucosamine, mannose, and muramic acid, sialic acids and N-acetyl galactosamine, although other saccharide monomer subunits known in the literature of glycosylated proteins may be present. Chemical linkages typically encompass glycosylated proteins comprising O-linked sugar residues, such as O-linked N-acetyl glucosamine. Each of the described glycosyl groups is susceptible to β -elimination from the protein to which it is bound under the conditions under which the mixture is contacted with the resin (page 17, lines 20-31).

With regard to multiple glycosylation sites, the specification indicates that the target protein typically comprises "at least one glycosyl group bound to a protein" (page 17, line 21). The claimed method does not recite isolating a protein by way of β -elimination solely at a single, specific site on a multiply glycosylated target. As such, it is unclear why the Examiner seems to imply that multiple glycosylation sites would be a disadvantage for the present method; indeed, the Applicants respectfully submit that such multiple sites, each of which can include targets for β -elimination, would presumably constitute an advantage to the claimed method.

In summary, the Applicants submit that, given the field of the invention and the level of skill and knowledge in the art, there is no reason *a priori* to presume that the claimed method would not be capable of isolating any glycosylated protein likely to be found in any biological sample. Accordingly, the Applicants submit that the instant specification provides everything needed such that one of ordinary skill in the art can perform the method as claimed, and that it is therefore clear to one of skill that the Applicants did indeed have possession of the claimed method at the time of filing.

In light of the foregoing discussion, it is believed that the instant rejection has been adequately addressed. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the amendments and remarks above, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance.

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone John Brady at (408) 553-3584.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1078, order number 10030218-1.

Respectfully submitted,

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